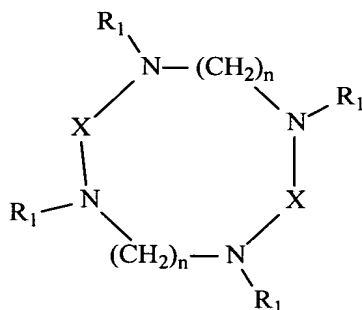


CLAIMS

What is claimed is:

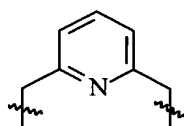
1. A complex comprising:
 - a) compound of formula (I):



(I)

wherein:

- each R_1 is independently hydrogen or (C_1-C_4) alkyl, optionally substituted with carboxy;
- each X is independently $(CH_2)_n$ or



- and each n is independently 2, 3, or 4;
- wherein the compound of formula I is substituted on one or more carbons other than a carbon of R_1 with one or more groups $-Y(PO_3H_2)_m$; wherein Y is a linker group; and m is 1, 2, 3, 4, 5, or 6; or a pharmaceutically acceptable salt thereof; and
- b) a detectable or therapeutic radionuclide.

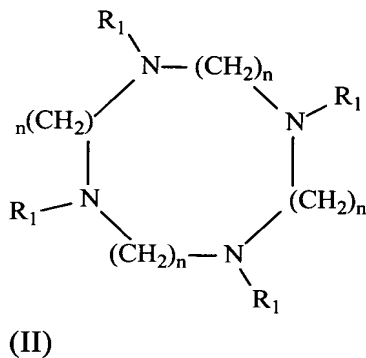
2. The complex of claim 1 wherein each R_1 is independently (C_1-C_4) alkyl, substituted with carboxy.
3. The complex of claim 1 wherein each R_1 is carboxymethyl or 2-
5 carboxyethyl.
4. The complex of claim 1 wherein each R_1 is carboxymethyl.
5. The complex of claim 1 wherein each n is independently 2 or 3.
10
6. The complex of claim 1 wherein each n is 2.
7. The complex of claim 1 wherein the linker group Y is about 5 angstroms to about 100 angstroms in length.
15
8. The complex of claim 1 wherein the linker group Y is about 10 angstroms to about 50 angstroms in length.
9. The complex of claim 1 wherein the compound of formula I is
20 substituted on a carbon other than a carbon of R_1 with one or two groups - $Y(PO_3H_2)_m$, wherein m is 1, 2, 3, 4, 5, or 6.
10. The complex of claim 1 wherein the linker group Y is an amino acid, a peptide, a saccharide, or a divalent (C_1-C_{10}) alkyl chain, optionally comprising
25 one or more non-peroxide oxy $(-O-)$, $-N(R_d)-$, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo $(=O)$, thioxo $(=S)$, or hydroxy, wherein R_d is hydrogen or (C_1-C_4) alkyl.
- 30 11. The complex of claim 10 wherein the linker group Y is an amino acid.

12. The complex of claim 11 wherein the amino acid is non-lipophilic.
13. The complex of claim 10 wherein the linker group Y is a saccharide.
- 5 14. The complex of claim 13 wherein the saccharide is a monosaccharide, disaccharide, or trisaccharide.
15. The complex of claim 13 wherein the saccharide is a polysaccharide.
- 10 16. The complex of claim 10 wherein the linker group Y is a peptide.
17. The complex of claim 16 wherein the peptide comprises 2 to 25 amino acid residues.
- 15 18. The complex of claim 17 wherein the amino acid residues are non-lipophilic.
19. The complex of claim 10 wherein the linker group Y is a divalent (C₁-C₁₀)alkyl chain, optionally comprising one or more non-peroxide oxy (-O-), -
20 N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.
20. The complex of claim 10 wherein the linker group Y is a divalent (C₁-
25 C₁₀)alkyl chain, comprising one or more non-peroxide oxy (-O-), -N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.
- 30 21. The complex of claim 10 wherein the linker group Y is a divalent (C₁-C₁₀)alkyl chain, optionally comprising one or more non-peroxide oxy (-O-), -

N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.

- 5 22. The complex of claim 10 wherein the linker group Y is a divalent (C₁-C₁₀)alkyl chain comprising one or more non-peroxide oxy (-O-), -N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.
- 10
23. The complex of claim 1 wherein each -Y(PO₃H₂)_m is independently 4-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-benzyl; 4-[4-(Bis-phosphonomethyl-carbamoyl)-butyrylamino]-benzyl; 4-(3,3-Bis-phosphono-propionylamino)-benzyl; 4-[4-(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-butyrylamino]-benzyl; 4-(3-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-2-{[2-(bis-phosphonomethyl-amino)-acetyl-amino]-methyl}-propionylamino)-benzyl; 4-(4-{Bis-[(bis-phosphonomethyl-carbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl; 4-{3-(3,3-Bis-phosphono-propionylamino)-2-[(3,3-bis-phosphono-propionylamino)-methyl]-[propionylamino]-benzyl; 4-(4-{Bis-[(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl; 4-{4-[(Bis-phosphono-methyl)-carbamoyl]-butyrylamino}-benzyl; or 4-[4-(Bis-{[(bis-phosphono-methyl)-carbamoyl]-methyl}-carbamoyl)-butyrylamino]-benzyl.
- 15
- 20

24. The complex of claim 1 wherein the compound of formula I is a compound of formula (II):



wherein:

- 5 each R_1 is independently hydrogen or (C_1-C_4) alkyl, optionally substituted with carboxy ($COOH$); and each n is independently 2, 3, or 4; wherein the compound of formula (II) is substituted on one or more carbons other than a carbon of R_1 with one or more groups $-Y(PO_3H_2)_m$; wherein Y is a linker group; and m is 1, 2, 3, 4, 5, or 6; or a pharmaceutically acceptable salt
- 10 thereof.

25. The complex of claim 24 wherein each R_1 is independently (C_1-C_4) alkyl, substituted with carboxy.

- 15 26. The complex of claim 24 wherein each R_1 is carboxymethyl.

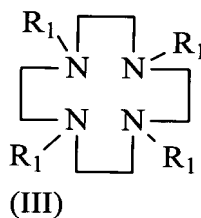
27. The complex of claim 24 wherein the compound of formula II is substituted on a carbon other than a carbon of R_1 with one or two groups - $Y(PO_3H_2)_m$.

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28. The complex of claim 24 wherein the compound of formula II is substituted on carbon with one group $-Y(PO_3H_2)_m$.

29. The complex of claim 24 wherein the linker group Y is an amino acid, a peptide, a saccharide, or a divalent (C₁-C₁₀)alkyl chain, optionally comprising one or more non-peroxide oxy (-O-), -N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with
 5 one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.
30. The complex of claim 24 wherein the linker group Y is a divalent (C₁-C₁₀)alkyl chain, optionally comprising one or more non-peroxide oxy (-O-), -
 10 N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.
31. The complex of claim 24 wherein each -Y(PO₃H₂)_m is independently 4-
 15 [2-(Bis-phosphonomethyl-amino)-acetylamino]-benzyl; 4-[4-(Bis-phosphonomethyl-carbamoyl)-butyrylamino]-benzyl; 4-(3,3-Bis-phosphono-propionylamino)-benzyl; 4-[4-(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-butyrylamino]-benzyl; 4-(3-[2-(Bis-phosphonomethyl-amino)-acetylamino]-2-
 20 {[2-(bis-phosphonomethyl-amino)-acetylamino]-methyl}-propionylamino)-benzyl; 4-(4-{Bis-[(bis-phosphonomethyl-carbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl; 4-{3-(3,3-Bis-phosphono-propionylamino)-2-[(3,3-bis-phosphono-propionylamino)-methyl]-[propionylamino]-benzyl; 4-(4-{Bis-[(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-methyl]-carbamoyl}-
 25 butyrylamino)-benzyl; 4-{4-[(Bis-phosphono-methyl)-carbamoyl]-butyrylamino}-benzyl; or 4-[4-(Bis-[(bis-phosphono-methyl)-carbamoyl]-methyl)-carbamoyl]-butyrylamino]-benzyl.

32. The complex of claim 1 wherein the compound of formula I is a compound of formula III:



wherein:

- each R_1 is independently hydrogen or (C_1-C_4) alkyl, optionally
- 5 substituted with carboxy (COOH); and wherein the compound of formula III is substituted on one or more carbons other than a carbon of R_1 with one or more groups $-Y(PO_3H_2)_m$; wherein Y is a linker group; and m is 1, 2, 3, 4, 5, or 6; or a pharmaceutically acceptable salt thereof.
- 10 33. The complex of claim 32 wherein each R_1 is independently (C_1-C_4) alkyl, substituted with carboxy.
34. The complex of claim 32 wherein each R_1 is carboxymethyl.
- 15 35. The complex of claim 32 wherein the compound of formula III is substituted with one or two groups $-Y(PO_3H_2)_m$.
36. The complex of claim 32 wherein the compound of formula III is substituted with one group $-Y(PO_3H_2)_m$.
- 20 37. The complex of claim 32 wherein the linker group Y is an amino acid, a peptide, a saccharide, or a divalent (C_1-C_{10}) alkyl chain, optionally comprising one or more non-peroxide oxy ($-O-$), $-N(R_d)-$, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with
- 25 one or more oxo ($=O$), thioxo ($=S$), or hydroxy, wherein R_d is hydrogen or (C_1-C_4) alkyl.

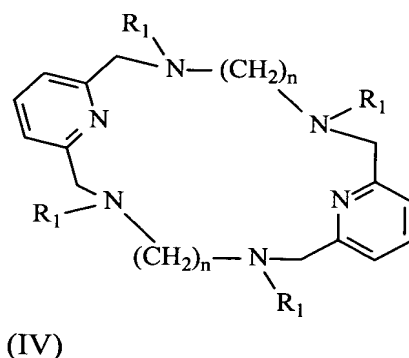
38. The complex of claim 32 wherein the linker group Y is a divalent (C_1 - C_{10})alkyl chain, optionally comprising one or more non-peroxide oxy (-O-), -N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C_1 - C_4)alkyl.

39. The complex of claim 32 wherein each $-Y(PO_3H_2)_m$ is independently 4-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-benzyl; 4-[4-(Bis-phosphonomethyl-carbamoyl)-butyrylamino]-benzyl; 4-(3,3-Bis-phosphono-propionylamino)-benzyl; 4-[4-(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-butyrylamino]-benzyl; 4-(3-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-2-[[2-(bis-phosphonomethyl-amino)-acetyl-amino]-methyl]-propionylamino)-benzyl; 4-(4-{Bis-[(bis-phosphonomethyl-carbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl; 4-{3-(3,3-Bis-phosphono-propionylamino)-2-[(3,3-bis-phosphono-propionylamino)-methyl]-[propionylamino]-benzyl; 4-(4-{Bis-[(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl; 4-{4-[(Bis-phosphono-methyl)-carbamoyl]-butyrylamino}-benzyl; or 4-[4-(Bis-[(bis-phosphono-methyl)-carbamoyl]-methyl)-carbamoyl]-butyrylamino]-benzyl.

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40. The complex of claim 32 wherein each R_1 is independently (C_1 - C_4)alkyl, substituted with carboxy (COOH); and wherein the ring is substituted on carbon with a group $-Y(PO_3H_2)_m$; or a pharmaceutically acceptable salt thereof.

41. The complex of claim 1 wherein the compound of formula I is a compound of formula IV:



5 wherein:

each R_1 is independently hydrogen or (C_1-C_4) alkyl, optionally substituted with carboxy (COOH); and each n is independently 2, 3, or 4; wherein the compound of formula IV is substituted on one or more carbons other than a carbon of R_1 with one or more groups $-Y(PO_3H_2)_m$; wherein Y is a linker group; and m is 1, 2, 3, 4, 5, or 6; or a pharmaceutically acceptable salt thereof.

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42. The complex of claim 41 wherein each R_1 is independently (C_1-C_4) alkyl, substituted with carboxy.

15 43. The complex of claim 41 wherein each R_1 is carboxymethyl.

44. The complex of claim 41 wherein the compound of formula IV is substituted with one or two groups $-Y(PO_3H_2)_m$.

20 45. The complex of claim 41 wherein the compound of formula IV is substituted with one group $-Y(PO_3H_2)_m$.

46. The complex of claim 41 wherein the linker group Y is an amino acid, a peptide, a saccharide, or a divalent (C_1-C_{10}) alkyl chain, optionally comprising

one or more non-peroxide oxy (-O-), -N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo (=O), thioxo (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.

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47. The complex of claim 41 wherein the linker group Y is a divalent (C₁-C₁₀)alkyl chain, optionally comprising one or more non-peroxide oxy (-O-), -N(R_d)-, or divalent aryl within the chain or at the terminus of the chain, which chain is optionally substituted on carbon with one or more oxo (=O), thioxo
10 (=S), or hydroxy, wherein R_d is hydrogen or (C₁-C₄)alkyl.

48. The complex of claim 41 wherein each -Y(PO₃H₂)_m is independently 4-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-benzyl; 4-[4-(Bis-phosphonomethyl-carbamoyl)-butyrylamino]-benzyl; 4-(3,3-Bis-phosphono-propionylamino)-benzyl; 4-[4-(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-butyrylamino]-benzyl; 4-(3-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-2-
15 {[2-(bis-phosphonomethyl-amino)-acetyl-amino]-methyl}-propionylamino)-benzyl; 4-(4-{Bis-[(bis-phosphonomethyl-carbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl; 4-{3-(3,3-Bis-phosphono-propionylamino)-2-[(3,3-bis-phosphono-propionylamino)-methyl]-[propionylamino]-benzyl; 4-(4-{Bis-[(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-methyl]-carbamoyl}-
20 butyrylamino)-benzyl; 4-{4-[(Bis-phosphono-methyl)-carbamoyl]-butyrylamino}-benzyl; or 4-[4-(Bis-[(bis-phosphono-methyl)-carbamoyl]-methyl)-carbamoyl]-butyrylamino]-benzyl.

25

49. The complex of claim 1 wherein the compound of formula I is
(6-{4-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-benzyl}-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetic acid;
(6-{4-[4-(Bis-phosphonomethyl-carbamoyl)-butyrylamino]-benzyl}-4,7,10-tris-
30 carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetic acid;

{3-[4-(3,3-Bis-phosphono-propionylamino)-benzyl]-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl}-acetic acid;

(4,7,10-Tris-carboxymethyl-3-{4-[4-(3-hydroxy-3,3-bis-phosphonopropyl-carbamoyl)-butyrylamino]-benzyl}-1,4,7,10-tetraaza-cyclododec-1-yl)-acetic

5 acid;

{3-[4-(3-[2-(Bis-phosphonomethyl-amino)-acetyl-amino]-2-{[2-(bis-phosphonomethyl-amino)-acetyl-amino]-methyl}-propionylamino)-benzyl]-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl}-acetic acid;

{6-[4-(4-{Bis-[(bis-phosphonomethyl-carbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl]-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl}-acetic acid;

[3-(4-{3-(3,3-Bis-phosphono-propionylamino)-2-[(3,3-bis-phosphono-propionylamino)-methyl]-propionylamino}-benzyl)-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl]-acetic acid;

15 {6-[4-(4-{Bis-[(3-hydroxy-3,3-bis-phosphono-propylcarbamoyl)-methyl]-carbamoyl}-butyrylamino)-benzyl]-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl}-acetic acid;

[6-(4-{4-[(Bis-phosphono-methyl)-carbamoyl]-butyrylamino}-benzyl)-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl]-acetic acid; or

20 (6-{4-[4[(Bis-[(bis-phosphono-methyl)-carbamoyl]-methyl]-carbamoyl]-butyrylamino]-benzyl}-4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetic acid.

50. The complex of claim 1 which comprises a detectable radionuclide.

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51. The complex of claim 50 wherein the detectable radionuclide is Technetium-99m, Ruthenium-97, Indium-111, Gallium-67 or -68, or Lead-203.

52. The complex of claim 1 which comprises a therapeutic radionuclide.

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53. The complex of claim 52 wherein the therapeutic radionuclide is Holmium-166, Yttrium-90, Samarium-153, or Gadolinium-159.

54. The complex of claim 52 wherein the therapeutic radionuclide is
5 Holmium-166.

55. A method for detecting the presence or absence of a calcified tissue target site within a mammal, comprising:

administering to the mammal a detectable dose of a complex of
10 claim 50; and
detecting the compound in the mammal to determine the presence or absence of the target site.

56. A therapeutic method for suppressing bone marrow in a mammal in need
15 of such therapy comprising administering to the mammal, an effective bone marrow suppressing amount of a complex of claim 52.

57. A therapeutic method for treating cancer in a mammal in need of such therapy comprising administering to the mammal, an effective amount of a
20 complex of claim 52.

58. A therapeutic method for treating bone pain in a mammal in need of such therapy comprising administering to the mammal, an effective amount of a complex of claim 52.

25

59. A therapeutic method for treating a bone related disease in a mammal in need of such therapy comprising administering to the mammal, an effective amount of a complex of claim 52.

30 60. The method of claim 59 wherein the bone related disease is an immunological disorder, a metabolic disease, an infection, an infectious disease,

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an inflammatory disease, a hematopoietic disorder, or a condition treatable with stem cell transplantation, with or without gene therapy, that utilize bone marrow ablation.

- 5 61. The method of claim 59 wherein the disease is Crohn's disease, rheumatoid arthritis, multiple sclerosis, osteoporosis, osteopenia, osteomyelitis, Paget's disease, sickle cell anemia, or a lysosomal or peroxisomal storage disease.

- 10 62. A pharmaceutical composition comprising the complex of claim 1 and a pharmaceutically acceptable carrier.

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